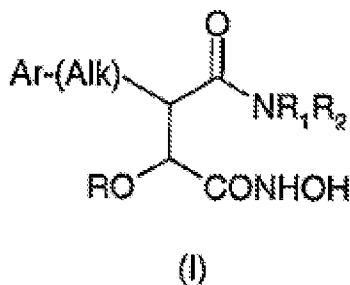


The listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of formula (I), or an enantiomer or diastereoisomer thereof, or a salt, ~~hydrate or solvate~~ thereof:



wherein Ar represents an optionally substituted phenyl;

R represents hydrogen or C₁-C₆ alkyl, or C₃-C₆ cycloalkyl;

Alk represents a divalent C₁-C₅ alkylene or C₂-C₅ alkenylene radical; and

R₁ and R₂ taken together with the nitrogen atom to which they are attached form a piperazinyl ring optionally substituted by at least one group of formula (II):



wherein m, p and n are independently 0 or 1;

Z represents, hydrogen, or an optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms which is optionally fused to another optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms;

Alk¹ and Alk² independently represent optionally substituted divalent C₁-C₃ alkylene radicals;

X represents -O-, -S-, -S(O)-, -S(O₂)-, -C(=O)-, -NH-, -NR₃-,
-S(O₂)NH-, -S(O₂)NR₃-, -NHS(O₂)-, or -NR₃S(O₂)-, where R₃ is C₁-C₃ alkyl; and

optionally substituted means at least one substituent selected from (C₁-C₆)alkyl, (C₁-C₆)alkoxy, hydroxy, hydroxy(C₁-C₆)alkyl, mercapto, mercapto(C₁-C₆)alkyl, (C₁-C₆)alkylthio, halo, trifluoromethyl, trifluoromethoxy, nitro, nitrile (-CN), oxo, phenyl, -COOH, -COOR^A, -COR^A, -SO₂R^A, -CONH₂, -SO₂NH₂, -CONHR^A, -SO₂NHR^A, -CONR^AR^B, -SO₂NR^AR^B, -NH₂, -NHR^A, -NR^AR^B, -OCONH₂, -OCONHR^A, -OCONR^AR^B, -NHCOR^A, -NHCOOR^A, -NR^BCOOR^A, -NHSO₂OR^A, -NR^BSO₂OR^A, -NHCONH₂, -NR^ACONH₂, -NHCONHR^B, -NR^ACONHR^B, -NHCONR^AR^B or -NR^ACONR^AR^B wherein R^A and R^B are independently a (C₁-C₆)alkyl or phenyl group.

2. (Original) A compound as claimed in claim 1 wherein R is hydrogen.
3. (Original) A compound as claimed in claim 1 wherein R is methyl.
4. (Original) A compound as claimed in claim 1 wherein R is ethyl, n-propyl, isopropyl, n-, sec- or tert-butyl, cyclopropyl, or cyclopentyl.
5. (Previously Presented) A compound as claimed in Claim 1 wherein Ar is substituted by at least one substituent selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, hydroxy, hydroxy(C₁-C₃)alkyl, mercapto, mercapto(C₁-C₃)alkyl, (C₁-C₃)alkylthio, halo, trifluoromethyl, trifluoromethoxy, nitro, nitrile (-CN), -COOH, -COOR^A, -COR^A, -SO₂R^A, -CONH₂, -SO₂NH₂, -CONHR^A, -SO₂NHR^A, -CONR^AR^B, -SO₂NR^AR^B, -NH₂, -NHR^A, -NR^AR^B, -OCONH₂, -OCONHR^A, -OCONR^AR^B, -NHCOR^A, -NHCOOR^A, -NR^BCOOR^A, -NHSO₂OR^A, -NR^BSO₂OR^A, -NHCONH₂, -NR^ACONH₂, -NHCONHR^B, -NR^ACONHR^B, -NHCONR^AR^B, or -NR^ACONR^AR^B wherein R^A and R^B are independently C₁-C₃ alkyl, phenyl or a 5- or 6-membered monocyclic aryl or heteroaryl ring.
6. (Previously Presented) A compound as claimed in claim 5 wherein the phenyl ring is substituted in the 4- position.

7. (Canceled)

8. (Previously Presented) A compound as claimed in Claim 1 wherein optional substituents in Ar are selected from methoxy, ethoxy, trifluoromethoxy, methyl, ethyl, trifluoromethyl, hydroxyl, mercapto, fluoro, chloro, and bromo.

9. (Original) A compound as claimed in claim 1 wherein Ar is 4-(C₁C₃alkoxy)phenyl.

10. (Previously Presented) A compound as claimed in claim 1 wherein Ar is 4-ethoxyphenyl.

11. (Previously Presented) A compound as claimed in Claim 1 wherein Alk is -CH₂-, -CH₂CH₂-, -CH₂CH(CH₃)-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-, -CH=CH-, -CH₂CH=CH-, -CH₂CH=CHCH₂-, or -CH=CHCH=CH-.

12. (Canceled)

13. (Canceled)

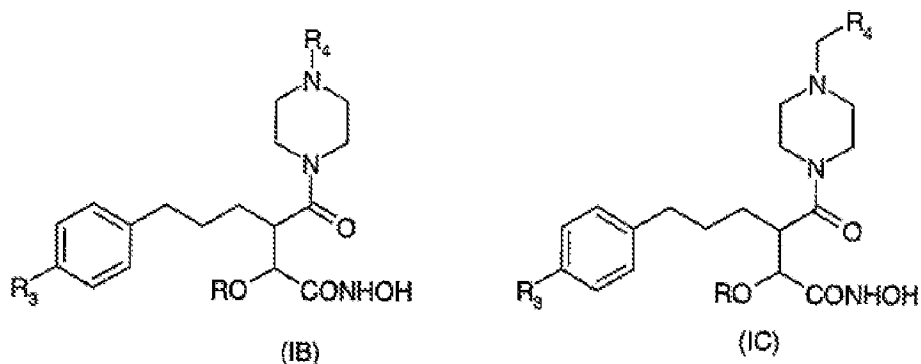
14. (Previously Presented) A compound as claimed in Claim 1 wherein in the group (II), when present, p is 0, Z is hydrogen and at least one of n and m is 1.

15. (Previously Presented) A compound as claimed in Claim 1 wherein in the group (II), when present, m, n and p are all 0 and Z is a carbocyclic or heterocyclic ring directly linked to a ring carbon or ring nitrogen of the -NR₁R₂ group.

16. (Previously Presented) A compound as claimed in Claim 1 wherein in the group (II), when present, p is 0, at least one of m and n is 1, and Z is a carbocyclic or heterocyclic ring linked to a ring carbon or ring nitrogen of the -NR₁R₂ group via a C₁-C₆ alkylene linker between Z and the -NR₁R₂ ring.

17. (Previously Presented) A compound as claimed in Claim 1 wherein in the group (II), when present, p is 1.

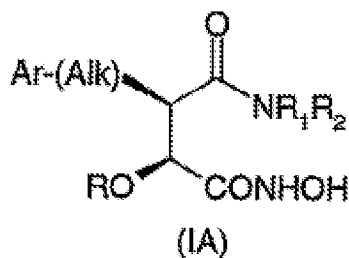
18. (Currently Amended) A compound as claimed in claim 1 of formula (1B) or (IC) or an enantiomer or diastereoisomer thereof, or a salt, ~~hydrate or solvate~~ thereof:



wherein R is hydrogen or methoxy, R₃ is trifluoromethyl, trifluoromethoxy C₁-C₃ alkoxy, hydroxy, or halo; R₄ is (i) -SO₂R₅ or -COR₅ wherein R₅ is C₁-C₆ alkyl or phenyl or monocyclic heteroaryl having 5 or 6 ring atoms, optionally substituted by (C₁-C₃)alkyl, (C₁-C₃)alkoxy, hydroxy, hydroxy(C₁-C₃)alkyl, mercapto, mercapto(C₁-C₃)alkyl, (C₁-C₃)alkylthio, halo, trifluoromethyl, trifluoromethoxy or (ii) phenyl or monocyclic heteroaryl having 5 or 6 ring atoms; optionally substituted by (C₁-C₃)alkyl, (C₁-C₃)alkoxy, hydroxy, hydroxy(C₁-C₃)alkyl, mercapto, mercapto(C₁-C₃)alkyl, (C₁-C₃)alkylthio, halo, trifluoromethyl, trifluoromethoxy.

19. (Original) A compound as claimed in claim 18 wherein a heteroaryl ring forming part of R₄ is pyridyl, pyrimidinyl, triazinyl, thienyl, or furanyl.

20. (Previously Presented) A compound as claimed in Claim 1 having the stereochemical configuration shown in formula (IA):



21. (Currently Amended) A compound as claimed in claim 1, which is selected from the group consisting of:

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

3R-(4-benzo[1,3]dioxol-5-ylmethyl-piperazine-1-carbonyl)-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-ylmethyl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-benzylpiperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyrimidin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethyl-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-chloro-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-[4-(4,6-dimethoxy-[1,3,5]triazin-2-yl)-piperazine-1-carbonyl]-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-trifluoromethyl-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-(4-benzyl-3RS-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S hydroxy-hexanoic acid hydroxyamide;

3R-(3S-4-dibenzyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxyhexanoic acid hydroxyamide;

3R-(4-benzyl-3RS-phenyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

4-(4-benzo[1,3]dioxol-5-ylmethyl-piperazin-1-yl)-2S, N-dihydroxy-4-oxo-3R-(4-trifluoromethoxy-benzyl)-butyramide;

4-(4-benzo[1,3]dioxol-5-ylmethyl-piperazin-1-yl)-3R-(4-benzyloxy-benzyl)2S, N-dihydroxy-4-oxo-butyramide;

6-(3, 5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

3R-(2S-benzyl-4-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethoxy-benzenesulfonyl)piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(toluene-4-sulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-[4-(5-bromo-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-[4-(5-benzenesulfonyl-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-[4-(4-butoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-2,3, 6-trimethylbenzenesulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-[4-(3,4-dimethoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-methoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-methoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid

hydroxyamide;

6-(4-fluoro-phenyl)-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-fluoro-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester;

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester;

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester;

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester;

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester;

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester; and

6-(4-ethoxy-phenyl)-2S-methoxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

22. (Previously Presented) A pharmaceutical composition comprising a compound as claimed in Claim 1, together with a pharmaceutically acceptable carrier.

23. (Canceled)

24. (Currently Amended) A method of treatment ~~or prophylaxis~~ of arthritis in mammals, which method comprises administering to the mammal an effective amount of a compound as claimed in Claim 1.

25. (Canceled)

26. (Previously Presented) A method as claimed in claim 24 wherein the arthritis is selected from rheumatoid arthritis, septic arthritis, osteoarthritis, or psoriatic arthritis;.

Claims 27-30 (Canceled)